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(71) Applicant: BAYER AG

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D-5090 Leverkusen 1 Bayerwerk(DE)

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(72) Inventor: Rosentreter, Ulrich, Dr.

Kondorweg 23

D-5600 Wuppertal 1(DE)

Inventor: Kluender, Harold, Dr.

65 Ocean Ave

West Haven, CT 06516(US)

Inventor: Abram, Trevor S., Dr.

214 Marlow Bottom

Marlow Bucks(US)

Inventor: Norman, Peter, Dr.

4 St Andrews Way Cippenham

Slough Berks, SL1 5NX(GB)

Inventor: Tudhope, Stephen R., Dr.

47 Kentons Lane

Windsor Berks, SL4 4JH(GB)

(54) Alkenoic acid derivatives.

(57) New alkenoic acid derivatives can be prepared by reaction of corresponding aldehydic esters with phosphorous compounds in inert solvents and in the presence of bases followed by hydrolysis of the intermediate esters. The new alkenoic acid derivatives can be used as active compounds in medicaments.

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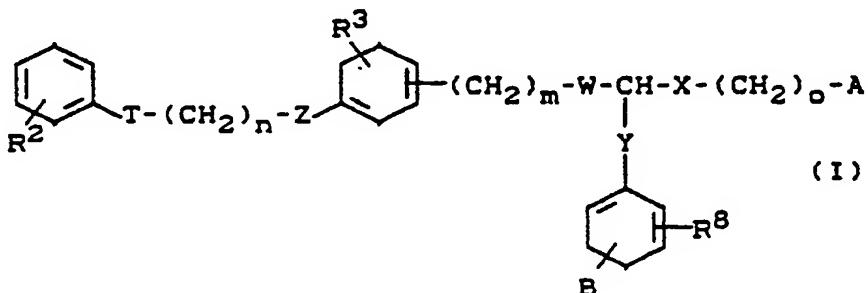
-NaCl 137, MgCl₂ 2.1, KCl 2.7, NaH₂DO₄ 0.5, CaCl₂ 2.4, NaHCO₃ 11.9, D-glucose 9.2.

Results

Contractions were normalised to the histamine-induced maximum for each preparation. The responses to analogue, LTD₄ and LTD₄ plus analogue were then expressed as a percentage of the maximum LTD₄ response in the appropriate control preparation. EC₅₀ (that concentration required to induce a 50% maximal LTD₄ response) values for 'test' and control tissues were calculated using a least squares linear regression program. These values were used to calculate a pK_B to qualify the degree of antagonism where appropriate.

Claims

15 1. Alkenoic acid derivatives of the general formula



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in which

30 X and Y are identical or different and represent sulfur, sulfoxide, sulfone, an alkylene chain, -SCH₂-, or oxygen or a direct bond,

W represents -CH=CH- or -CH₂-CH₂-

o represents a number 1 to 5

35 A and B are identical or different and represent carboxyl, carboxymethylene, tetrazolyl or tetrazolyl-methylene, or -CO₂R⁹ or -CH₂CO₂R⁹ or -CONR¹⁰R¹¹ or nitrile

n represents a number 1 to 10,

m represents a number 0 to 7,

T and Z are identical or different and represent oxygen or a direct bond
and

40 R², R³, R⁸ are identical or different and represent hydrogen, alkyl, alkoxy, halogen, trifluoromethyl, trifluoromethoxy, cyano or nitro

R⁹ is lower alkyl and R¹⁰ and R¹¹ are hydrogen, lower alkyl, alkylsulfonyl or arylsulfonyl or together are an alkylene chain to form a ring
and their salts have been prepared.

45 2. Alkenoic acid derivatives according to claim 1, wherein

X and Y are identical or different and represent sulfur, sulfoxide, sulfone, a methylene group, -SCH₂-, oxygen, an ethylene group or a direct bond,

W represents -CH=CH- or -CH₂CH₂-

o represents a number 1 to 4,

50 n represents a number 1 to 7,

m represents a number 0 to 5,

T and Z are identical or different represent oxygen or a direct bond

and

55 R², R³, R⁸ are identical or different and represent hydrogen, lower alkyl, lower alkoxy, fluorine, chlorine or trifluoromethyl
and their salts.

3. Alkenoic acid derivatives according to claims 1 and 2, where in
 X represents sulfur, sulfon or a methylene group,
 Y represents sulfur, a methylene group, -SCH₂- or a direct bond,
 W represents -CH=CH-,

5 R⁸ and R³ represent H,

R² represents H or F,

o represents a number 1, 2, 3 or 4,

n represents a number 2, 3, 4, 5 or 6,

m represents a number 0, 1 or 2,

10 T represents oxygen or a direct bond

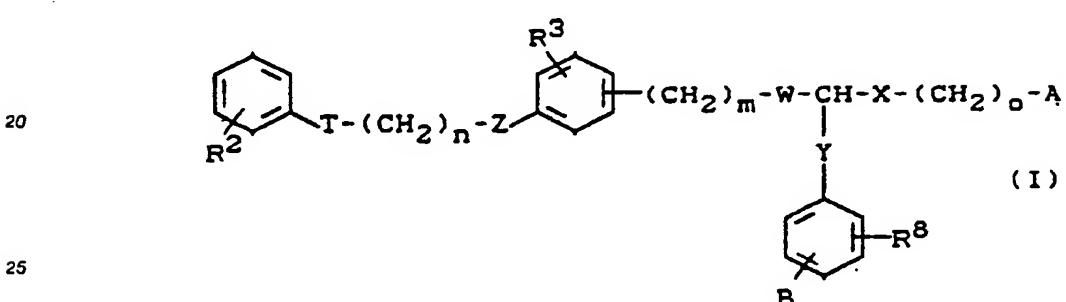
Z represents oxygen or a direct bond

A represents carboxyl or ester thereof,

B represents para carboxyl or ester thereof, and their salts.

4. Alkenoic acid derivatives according to claims 1 to 3 for therapeutic treatment.

15 5. Process for the preparation of alkenoic acid derivatives of the formula



in which

30 X and Y are identical or different and represent sulfur, sulfoxide, sulfone, an alkylene chain, -SCH₂-, oxygen or a direct bond,

W represents -CH=CH- or -CH₂-CH₂-

o represents a number 1 to 5

35 A and B are identical or different and represent carboxyl, carboxymethylene, tetrazoyl or tetrazoylmethylene, or -CO₂R⁹ or -CH₂CO₂R⁹ or -CONR¹⁰R¹¹ or nitrile wherein R⁹ is lower alkyl and R¹⁰ and R¹¹ are hydrogen, lower alkyl, alkylsulfonyl or arylsulfonyl or together are an alkylene chain to form a ring.

n represents a number 1 to 10,

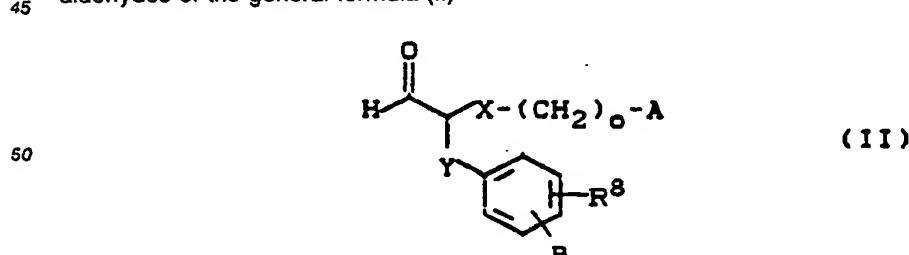
m represents a number 0 to 7,

40 T and Z are identical or different and represent oxygen or a direct bond
and

R², R³, R⁸ are identical or different and represent hydrogen, alkyl, alkoxy, halogen, trifluoromethyl, trifluoromethoxy, cyano or nitro

and their salts, characterized in that

45 aldehydes of the general formula (II)



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in which

X, Y, o and R⁸ have the above mentioned meaning and

A and B are identical or different and represent CO₂R⁹ or CH₂CO₂R⁹ or CONR¹⁰R¹¹ or nitrile where in R⁹

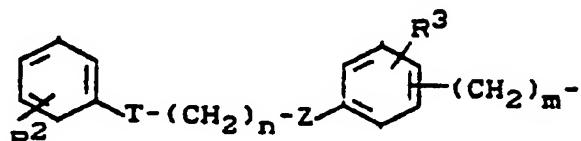
represents lower alkyl and R¹⁰ and R¹¹ represent lower alkyl, a methylene chain or H,
are reacted with phosphorus compounds of the general formula (III)



in which

5 R¹ is

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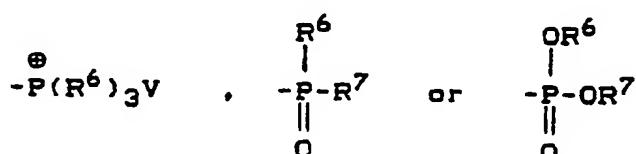
in which

15 R², T, n, Z, R³ and m have the above mentioned meaning

and

U represents a group of the formula

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where

R⁶ and R⁷ are identical or different and denote alkyl or phenyl

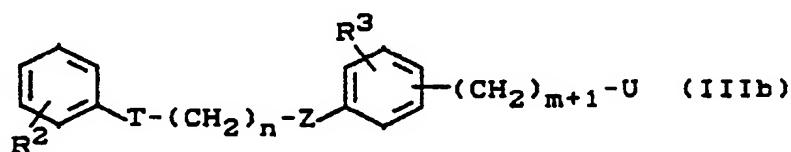
and

V denotes a halide anion or a tosylate anion in inert solvents in the presence of bases, whereby the esters
30 are then hydrolysed or partially hydrolysed.

6. Process according to claim 5, characterised in that it is carried out in the temperature range from
-80 °C to +70 °C.

7. Phosphorous compounds of the formula

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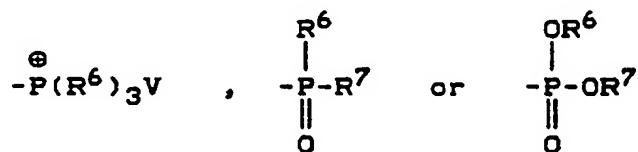
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wherein

R² and R³ are identical or different and represent hydrogen, alkyl, alkoxy, halogen, trifluoromethyl,
45 trifluoromethyl, cyano or nitro,

U represents a group of the formula

50



55 where

R⁶ and R⁷ are identical or different and denote alkyl or phenyl
and

V denotes a halide anion or tosylate anion.

T and Z are identical or different and represent oxygen or a direct bond,
m represents a number 0 to 7 and
n represents a number 1 to 10.

- 5 8. Medicaments containing alkenoic acid derivatives according to claims 1 to 3.
 9. Medicaments according to claim 8, characterised in that it contains about 0.5 to 98% by weight of
 the alkenoic acid derivatives.
 10. Use of alkenoic acid derivatives according to claims 1 to 3 for the preparation of medicaments.
 11. Use according to claims 9 and 10, for the preparation of medicaments for the treatment of deseases
 of the circulatory system and of the respiratory system.

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DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int. Cl 4)
D, A	GB - A - 2 184 121 (LILLY) * Claims; abstract; pages 4, 5 *	1, 5, 7, 8-11	C 07 C 63/66 C 07 C 65/28 C 07 C 69/94 C 07 F 9/28 C 07 C 51/00 C 07 C 67/00 C 07 C 149/273 A 61 K 31/19 A 61 K 31/235
A	EP - A2 - 0 084 667 (BASF) * Claims; page 9 *	1, 5, 7, 8-10	
TECHNICAL FIELDS SEARCHED (Int. Cl 4)			
C 07 C 63/00 C 07 C 65/00 C 07 C 69/00 C 07 C 149/00			
The present search report has been drawn up for all claims			
Place of search	Date of completion of the search	Examiner	
VIENNA	09-08-1989	HOFBAUER	
CATEGORY OF CITED DOCUMENTS		T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document	
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A : technological background	O : non-written disclosure		
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